Oath or declaration

The PTO stated that the oath or declaration was defective because the declaration was not signed. Enclosed herewith is a declaration signed by the inventor identifying the present application by application number and filing date.

Sequence listing

The PTO stated that the application did not comply with the sequence rules set forth in 37 CFR §§1.821-1.825 because the application does not contain a paper copy or computer readable form (CRF) of a sequence listing containing the peptides set forth on page 38 of the specification. Enclosed herewith is a paper copy and CRF of the sequence listing. The contents of the paper copy and CRF are identical and list the three peptide sequences found on page 38 of the specification. Thus, no new matter has been added.

35 U.S.C. §103

The PTO rejected Claims 1-7 as being unpatentable over Bona et al. (*Cell Mol. Biol.* **40(Suppl. I)**:21-30, 1994) in view of Liu et al. (*Int. Immunol.* 7:1255-1263, 1995). The PTO held that Bona et al. teach a fusion protein comprising an IgG with its CDR3 region replaced by a viral T cell peptide which specifically stimulates T cells. According to the PTO, the claimed invention differs from the prior art teachings by the recitations of using T cell receptor peptide agonists derived from proteolipid or myelin basic protein. The PTO concludes that it would have been obvious to substitute the viral peptides of Bona et al. for the proteolipid and myelin basic proteins disclosed by Karpus et al. and Liu et al., respectively.

As acknowledged by the PTO at page 3 of the Office Action, the peptides of Bona et al. specifically stimulate T cells. In contrast, Claim 1 as amended recites a T cell receptor peptide antagonist rather than an agonist. These antagonist peptides treat autoimmune disorders by inhibiting T cells. Liu et al. and Karpus et al. disclose particular peptides, but neither disclose nor suggest that they inhibit T cells. In order to support a finding of *prima facie* obviousness, the cited references must provide suggestion or motivation to combine. Because none of the cited references relate to T cell receptor peptide antagonists, which inhibit T cell function, for treatment of autoimmune diseases by inhibiting T cells, there is no *prima facie* case of obviousness.

The PTO cited a section of Bona et al. which states that the method of delivering antigens to cells via IG's "can be extended to express other biologically important epitopes such as tumor antigens,

oncogenes or self antigens which can be used in the antitumor therapy or the therapy of autoimmune disease." The idea presented by Bona et al. is to displace autoantigenic self peptides from MHC molecules so that T cells cannot engage a specific self peptide-MHC complex and will not be activated. Bona et al. cite a paper by Adorini et al. (*Immunol. today* **11**:383-386) which describes the MHC peptide competition strategy for treatment of autoimmunity. In contrast, the present invention demonstrates how the claimed antagonist peptides form complexes that engage pathogenic T cells in order to generate a negative signal and inactivate the cells. Thus, the present method differs from that of Bona et al. in that the claimed molecule engages T cells, while the molecule of Bona does not engage T cells. In the present invention, down regulation of the T cell receptor occurs such that T cells will not be activated even if the self peptide again becomes available. In contrast, the T cells in Bona et al. will become activated if the self peptide becomes available.

In view of the comments presented above, Applicant respectfully requests withdrawal of the rejections under 35 U.S.C. §103

Conclusion

Applicant submits that all claims are in condition for allowance. However, if minor matters remain, the Examiner is invited to contact the undersigned at the telephone number provided below.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 5-18-00

By: _____

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051000

Application No.: 09/111,123

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990. Specifically the peptides on page 38
- [X] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [X] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [ ] 7. Other: _____

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

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